

**Amendments to the Specification:**

Please amend the paragraph on page 14, line 31 to page 15, line 5 as follows:

**Figure 1.** siRNA-mediated inhibition of Livin expression. (a) Predicted secondary structure of pSUPER-Livin-1 and pSUPER-Livin-2 transcripts (**SEQ ID NOS 12 & 13 respectively in order of appearance**). (b) Western blot analysis of Livin protein expression in MeWo melanoma, H1299 lung cancer and HeLa cervical carcinoma cells. Tubulin: detection of  $\alpha$ -Tubulin protein expression to monitor equal loading between individual lanes. (c) Inhibition of Livin protein expression in HeLa cells by pSUPER-Livin-1 and pSUPER-Livin-2. Control vector pSUPER-Luc expresses siRNA targeting the *P. pyralis* luciferase gene. (d) Reduction of livin transcripts in HeLa cells by siRNA targeting of livin. Northern blot analysis of poly-A<sup>+</sup>-RNA isolated from HeLa cells transfected with pSUPER-Livin-1, pSUPER-Livin-2, or control transfected HeLa cells, respectively. GAPDH: detection of glyceraldehyde-3-phosphate dehydrogenase transcripts.

Please amend the paragraph on page 15, lines 7-14 as follows:

**Figure 2.** siRNA against Livin increases Caspase-3 activities in HeLa cells. Livin-positive HeLa and Livin-negative H1299 cells were transfected with either pSUPER-Livin-2 or control vector pSUPER-Luc. DEVD-pNA (**peptide disclosed as SEQ ID NO: 14**) hydrolysis was measured in cytosolic extracts 48 hours post-transfection. Indicated are the Caspase-3 activities of pSUPER-Livin-2-transfected cells relative to control transfectants (pSUPER-Luc), arbitrarily set at 1.0. Values represent the means obtained from at least three independent transfections, error bars indicate the standard deviations. Inclusion of the specific Caspase-3 inhibitor DEVD-fmk (**peptide disclosed as SEQ ID NO: 14**) blocks pSUPER-Livin-2-induced hydrolysis of DEVD-pNA (**peptide disclosed as SEQ ID NO: 14**).

Please amend the paragraph on page 17, line 33 to page 18, line 10 as follows:

Since pSUPER-Livin-2 regularly suppressed endogenous Livin expression more strongly than pSUPER-Livin-1 (Figure 1), the former was chosen for subsequent analyses. It has been

reported that Livin inhibits Caspase-3 activities following ectopic expression from heterologous promoters or in *in vitro* assays. In contrast to these studies, the siRNA approach followed in this study should allow to analyze the effects of endogeneous Livin on cellular Caspase-3 activities. As shown in Figure 2, pSUPER-Livin-2 increased Caspase-3-like activities in HeLa cells, indicating that the down-regulation of Livin expression is associated with a release of Caspase-3 from negative regulation by Livin. This conclusion is corroborated by the observation that the Caspase-3 inhibitor DEVD-fmk (peptide disclosed as SEQ ID NO: 14) completely inhibited the increase of DEVD-cleavage (peptide disclosed as SEQ ID NO: 14) following pSUPER-Livin-2 transfection in HeLa cells (Figure 2). In further support for the specificity of the Livin-targeting siRNAs, induction of caspase-3 activities by pSUPER-Livin-2 was observed in Livin-expressing HeLa cells, but not in H1299 cells (Figure 2) which do not express endogeneous Livin protein (Figure 1b).

Please amend the paragraph on page 21, lines 25-33 as follows:

Sequence (~~nucleotides 648-668 of SEQ ID NO:11~~):

Livin: ggaagagactttgtccacagt (nucleotides 648-668 of SEQ ID NO:11) GRDFVHS (SEQ ID NO: 15)

LivinMT: ggcagggatttcgtgcattcc (SEQ ID NO: 16) GRDFVHS (SEQ ID NO: 15)

Comparison of livin and livinMT DNA and protein sequences (bold nucleotides represent mutations):

Livin: ggaagagactttgtccacagt (nucleotides 648-668 of SEQ ID NO:11) GRDFVHS (SEQ ID NO: 15)

LivinMT: **ggcagggatttcgtgcattcc** (SEQ ID NO: 16) GRDFVHS (SEQ ID NO: 15)

Please amend the paragraph on page 22, lines 6-31 as follows:

This could not be achieved with pLivin-alphaMT.

livin-alpha (SEQ ID NO: 10)

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1 gtctggtggc aggccctgtgc ctatccctgc tgtccccagg gtggggccccc ggggtcagga
 61 gctccagaag ggccagctgg gcatattctg agattggcca tcagccccca tttctgctgc
121 aaacctgtgc agagccagtg ttccctccat gggacctaataa gacagtgcctaa agtgctgtca
181 ccgtggacca cagccgagcc actgggcagc cggtgatggt cccacgcagg agcgctgtgg
241 accccgcctt ctgggcagcc ctgtccttagg cctggacacc tgcagagccctt gggaccacgt
301 ggatgggcag atccctgggcc agctgcggcc cctgacagag gaggaagagg aggagggcgc
361 cggggccacc ttgtccaggg ggcctgcctt cccggcatg ggctctgagg agttgcgtct
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421 ggcctccccc tatgactggc cgctgactgc tgagggtgcca cccgagctgc tggctgctgc  
481 cggcttcac cacacaggcc atcaggacaa ggtgagggtgc ttcttctgat atgggggcct  
541 gcagagctgg aagcgcgggg acgaccctg gacggagcat gccaagtgg tccccagctg  
601 tcagttctg ctccggtaaa aaggaagaga ctttgccac agtgtgcagg agactcactc  
661 ccagctgctg ggctctggg acccggtggaa agaaccggaa gacgcagccc ctgtggcccc  
721 ctccgtccct gcctctgggt accctgagct gcccacaccc aggagagagg tccagctgta  
781 aagtgcggc gagccaggag gggtcagttc agcccaggcc cagagggcgt ggtgggtct  
841 tgagccccc ggagccaggatgtggaggc gcagctgcgg cggctgcagg aggagaggac  
901 gtgcagggt tgccctggacc ggcgggtgtc catcgcttt gtgcgggtcg gccacctgg  
961 ctgtgctgatgtgatggccatc gctgcagct gtgcggccatc tgcagagccc cegtcggcag  
1021 cccgcgtgcgc accttcctgt cctaggccag gtgcgcattgc cggccagggtg ggctgcagag  
1081 tgggctccct gcccctctat gcctgttctg gactgtgttc tgggctctgat gaggatggca  
1141 gagctgggtt ccattccagca ctgaccagcc ctgattcccc gaccaccgc cagggtggag  
1201 aaggaggccc ttgcgttgcg tggggatgg cttaactgtat cctgtttgaa tgcttctgaa  
1261 tagaaataaa gtgggttttc cctggaggtaa aaaaaaaaaaaaaaa aa

Please amend the paragraph on page 23, lines 1-24 as follows:

livin-beta (SEQ ID NO: 11)

1 ccctggata ctccccccc aagggtgtctg gtggcaggcc tgcctatc cctgctgtcc  
61 ccagggtggg ccccgggggc caggagctcc agaaggggca gctggcata ttctgagatt  
121 ggccttcac ccccatatc gctgcatttc gtcggatcc tggtcagagc cagtgttccc tccatggac  
181 taaaagacag tgccaaatgc ctgcaccgtg gaccacagcc gagccactgg gcagccggtg  
241 atggtccac gcaggagcgc tggggatccc gctctctgg cagccctgtc ctaggcctgg  
301 acacctgcag agcctggac cacgtggatg ggcagatcct gggccagctg cggccctgt  
361 cagaggagga agaggaggag ggcggccggg ccaccttgc cagggggccgc gccttcccg  
421 gcatgggtc tgaggagttt cgtctggccct ctttctatga ctggccgctg actgctgagg  
481 tgccaccgc gctgctggct gctgcccgt tttccacac aggccatcag gacaaggta  
541 ggtgcttctt ctgcattggg ggcctgcaga gctggaaagcg cggggacgac ccctggacgg  
601 agcatgcac gtggttcccc agctgtcaat tccatgtccc gtcaaaagga agagacttt  
661 tccacatgtt gcaggagact cactcccacg tgcggatccc ctgggaccgc tggaaagaac  
721 cggaaagacgc agccctgtg gccccctccg tccctgcctc tgggtaccat gagctgccc  
781 caccaggag agaggatccag tctgaaatgt cccaggagcc aggagccagg gatgtggagg  
841 cgcagctgcg gcccgtgcag gaggagagga cgtcaaggt gtgcctggac cgcggcgtgt  
901 ccattcgatgtt tgcggatccc ggcacatgg tctgtgtca gtgtgcccccc ggcctgcac  
961 tgcggccatctgcagatcc cccgtccgc gccgcgtgcg cacatctgtc tccatggcca  
1021 ggtgccatgg ccggccagggt gggctgcaga gtgggttccc tgcctgttct  
1081 ggactgtgtt ctggccatgc tgaggatggc agagctgggtg tccatccagc actgaccagc  
1141 cctgattcccc cggaccacgc ccagggtgaa gaaggaggcc ttgcgttgcg gtggggatg  
1201 gcttaactgtt acctgtttgg atgcttctgaa atagaaataaa agtgggtttt ccctggaggt

Please amend the paragraph on page 25, lines 25-31 as follows:

To detect caspase-3 protease activities, the ApoAlert Caspase-3 Colorimetric Assay Kit (Clontech, Palo Alto, USA) was utilized. Cytosolic lysates were prepared 48 h following transfection and incubated with 50 µM p-nitroanilide (pNA) conjugated to the caspase cleavage site Asp-Glu-Val-Asp (DEVD) (**SEQ ID NO: 14**) for 1 h at 37° C. Hydrolyzed pNA was detected using a Multiscan MS colorimeter (ThermoLabsystems, Vantaa, Finland) at 405 nm. For control experiments, 10 µM of the Caspase-3 inhibitor DEVD-fmk (**peptide disclosed as SEQ ID NO: 14**) (Clontech) was included into the reaction, before addition of the substrate.